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ORIGINAL REPORT

PREDICTION OF GOOD FUNCTIONAL RECOVERY AFTER STROKE BASED ON COMBINED MOTOR AND SOMATOSENSORY EVOKED POTENTIAL FINDINGS

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Objective: **To delineate whether functional recovery after stroke, determined by the modified Rankin Scale during the neurologically stable chronic stage, is associated with the presence or absence of motor evoked potential or somatosensory evoked potential measured during the sub-acute stage at the commencement of rehabilitation.**

Design: **Retrospective medical records review.**

Patients: **Consecutive 105 first-ever unilateral patients after stroke.**

Methods: **Patients underwent motor evoked potential and somatosensory evoked potential studies at the commencement of rehabilitation (i.e. approximately 1 month post-onset), and functional recovery was measured using the modified Rankin Scale at 3 months post-onset. The independent abilities of motor evoked potentials and somatosensory evoked potentials for predicting good functional recovery (modified Rankin Scale ≤2) were determined by multivariable logistic regression analysis adjusted for age, laterality of lesion, and National Institute of Health Stroke Scale scores at onset of rehabilitation.**

Results: **The adjusted logistic regression model revealed that patients with negative motor evoked potential or somatosensory evoked potential responses in the lower limb were less likely to achieve good functional recovery (odds ratio = 0.057~0.099, $p < 0.05$) relative to positive motor evoked potential and somatosensory evoked potential responses in the lower limb.**

Conclusion: **Evoked potential studies measured at the commencement of rehabilitation could be used in a complementary manner to predict functional recovery after stroke.**

Key words: stroke; recovery; function; somatosensory evoked potential; motor evoked potential.

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INTRODUCTION

The prediction of post-stroke functional recovery is important in stroke rehabilitation. Several clinical and demographic factors have been suggested previously as predictors of functional recovery after stroke (1).

Evoked potential (EP) studies provide a useful, objective means of assessing the integrities of cortico-spinal and somatosensory pathways, and therefore, EP findings have prognostic value in terms of predicting post-stroke functional recovery (2, 3). However, previous reports either involved small number of subjects or did not evaluate motor EP (MEP) and somatosensory EP (SEP) simultaneously.

In the present study, we studied whether functional recovery after stroke, determined by the modified Rankin Scale (mRS) during the neurologically stable chronic stage, is associated with the presence or absence of MEP or SEP measured during the sub-acute stage at the commencement of rehabilitation.

PATIENTS AND METHODS

Patients

We reviewed the medical records of 191 consecutive patients with first-ever unilateral stroke who commenced rehabilitative training approximately one month (mean 25.9 standard deviation (SD) 14.3 days) post-onset onset at a university hospital during the 14-month period from January 2007 to February 2008. Stroke was diagnosed based on clinical history, a physical examination (by neurologists), and confirmation by brain magnetic resonance imaging (MRI).

The exclusion criteria applied were: (*i*) a recurrent stroke history; (*ii*) the presence of nonvascular brain lesions, such as, lesions due to traumatic injury, a brain tumour, or Parkinsonism; (*iii*) no functional deficit (mRS = 0); (*iv*) a bed-ridden status and an inability to tolerate rehabilitative training (mRS = 5); (*v*) a co-morbidity, such as peripheral polyneuropathy; (*vi*) a concomitant severe medical illness that could affect the prognosis; and (*vii*) those in whom an MEP study was contraindicated, for example, those with an implanted metallic device, such as aneurysmal clip or cardiac pacemaker, and those with a history of epilepsy or craniotomy.

Measurement of functional recovery after stroke

Motor function was measured at the commencement of rehabilitation at mean 25.9 (SD 14.3) days post-onset and during the neurologically stable chronic stage (mean 96.0 (SD 18.1) days post-onset) using the mRS. Rehabilitative training was routinely administered during admission to the rehabilitation unit, consisting of 1–1.5 h of physical therapy (mobility and gait training), 1–1.5 h of occupational therapy (task-oriented training and activities of daily living training), and/or 1 h of speech therapy on each therapy day, which was divided into 2 daily sessions, 5 days a week, according to the individual patient's needs.

The mRS is a clinician-reported measure of global disability with high validity and reliability (4) and is widely applied for evaluating stroke outcomes, degree of disability, and dependence with respect to the daily activities (5). We defined a good functional recovery as mRS 1 or 2 (6) out of 6 grades (0–5), where 0 corresponds to no symptoms and 5 to severe disability or a bedridden status (7). The protocol used was approved by the institutional review board of (our) institution.

Evoked potential studies

Neurophysiological measurements were carried out bilaterally on upper and lower limbs on the same day as mRS measurements. MEPs were measured in all 4 extremities (abductor pollicis brevis in upper limbs and the adductor hallucis in lower limbs) using a standard protocol (8). Reproducible responses with minimal peak to peak amplitude of 200 μV in at least 5 of 10 consecutive trials using a figure-of-eight coil were defined as a positive response ("MEP(+)"). SEPs were measured by stimulating median nerves at wrists and tibial nerves at ankles using a standard protocol (9). In cases with an amplitude (N1 to P1) difference of < 50% and a latency (N1) difference of < 10% compared with unaffected sides, the response was regarded as positive ("SEP(+)").

Statistical analysis

Baseline demographics, stroke factors, and the presence of an EP response were compared with respect to functional recovery status at 3 months post-onset (good recovery mRS ≤2 and poor recovery mRS >3). The independent effects of MEP and SEP on functional recovery were assessed using a multivariate logistic regression model, unadjusted or adjusted for 8 key prognostic factors, namely, sex, age, lesion location, lesion laterality, stroke type (ischaemic or haemorrhagic), the presence of diabetes mellitus, National Institute of Health Stroke Scale (NIHSS) at onset of rehabilitation, and for MEP and SEP responses. The adjusted model was developed by backward elimination using a significance level of 0.2 to enter and 0.05 to stay. Sex, lesion location, stroke type, and presence of diabetes mellitus were eliminated from the final adjusted regression model. The sensitivities and specificities of MEP and SEP for predicting a good functional recovery (mRS ≤2) were calculated. In addition, we also calculated the positive and negative predictive values of MEP and SEP.

All analyses were performed using SPSS 15.0 for Windows. Significance was accepted for < 0.05, and 95% confidence intervals (CI) are provided.

RESULTS

Of the 191 patients considered initially, 86 were excluded due to; recurrent stroke ($n = 38$), no or a severe functional deficit ($n = 28$), non-vascular brain lesions ($n = 13$), and diabetes mellitus requiring insulin therapy ($n = 7$). Thus, 105 patients constituted the study cohort. Baseline characteristics of the 105 subjects are shown in Table I.

Table I. *Baseline characteristics of subjects*

Characteristics	
Mean age, years, *n* (SD)	65.7 (14.3)
Sex, male/female, *n*	59/46
Stroke localization, *n*	
Cortical	7
Cortico-subcortical	16
Subcortical	44
Brain stem	19
Cerebellum	3
Multiple	16
Stroke type, *n*	
Ischaemic	85
Haemorrhagic	20
Stroke laterality, *n*	
Right hemisphere	54
Left hemisphere	51
mRS at onset of rehabilitation, mean (SD)	3.32 (0.88)
NIHSS at onset of rehabilitation, mean (SD)	6.16 (4.95)

mRS: modified Rankin Scale; NIHSS: National Institute of Health Stroke Scale; SD: standard deviation.

The mean mRS (from 3.32 (SD 0.88) to 2.47 (SD 1.19), $p < 0.001$ by paired *t*-test) and mean NIHSS (from 6.16 (SD 4.95) to 3.05 (SD 3.47), $p < 0.001$) significantly improved 3 months post-stroke from the rehabilitation start. Of the 105 patients, 53 patients (50.5%) achieved a good functional state at 3 months post-onset. By unadjusted analysis, patients older than 80 years were found to have a significantly lower odds ratio of achieving a good functional recovery than those younger than 50 years (unadjusted OR = 0.21, 95% CI = 0.05–0.93; $p = 0.024$). An NIHSS at onset of rehabilitation of ≥ 5 was found to be a significant predictor of a poor functional recovery (unadjusted OR = 0.11, 95% CI = 0.04–0.29; $p < 0.001$). Adjusted analysis also showed that age ≥ 80 years and an NIHSS at onset of rehabilitation ≥ 5 were significant predictors of a poor functional recovery (adjusted OR = 0.04, 0.06; $p = 0.020$, $p < 0.001$, respectively). Other demographic and stroke variables were not found to be significantly associated with recovery.

By unadjusted EP analysis, MEP(+) in a lower limb, SEP(+) in an upper and in a lower limb were found to be significantly associated with a better recovery than the corresponding negative responses (unadjusted OR = 0.34, 0.23, 0.17; $p = 0.008$, $p = 0.001$, $p < 0.001$, respectively). However, the presence of MEP and SEP responses were not found to be significantly associated with better recovery when the adjusted model was used.

We then applied cross-matched EP analysis. By unadjusted cross-matched EP analysis, the upper limb MEP(–)SEP(–) group had a significantly lower OR for a good recovery (unadjusted OR = 0.20, 95% CI 0.07–0.56; $p = 0.002$) than the MEP(+)SEP(+) group. Furthermore, the lower limb MEP(+) SEP(–), MEP(–)SEP(+), and MEP(–)SEP(–) groups had significant lower OR for a good recovery than the MEP(+)SEP(+) group (unadjusted OR = 0.19, 0.07, 0.07; $p = 0.016$, $p = 0.001$, $p < 0.001$, respectively).

By adjusted EP analysis, only cross-matched EP findings in a lower limb were found to be significantly associated with a good recovery. The lower limb MEP(+)SEP(–), MEP(–) SEP(+), MEP(–)SEP(–) groups had significantly lower OR than the MEP(+)SEP(+) group (adjusted OR = 0.09, 0.06, 0.10; $p = 0.033$, $p = 0.013$, $p = 0.040$, respectively) (Table II).

The relationship between a good functional recovery at 3 months post-onset and the results of EP studies at rehabilitation commencement are shown in Table III. Sensitivity and specificity for predicting a good functional recovery were 39.6% and 75.0% for upper limb MEP, 56.6% and 69.2% for lower limb MEP, 73.6% and 61.2% for upper limb SEP, and 71.2% and 70.8% for lower limb SEP, respectively.

DISCUSSION

The main finding of this study is that patients with a negative lower limb MEP or SEP response, and patients with negative

Table II. *Unadjusted and adjusted odds ratios (OR) of good functional recovery (mRS ≤2) at 3 months after stroke in 105 patients*

	n	Unadjusted OR* (95% CI)	*p*-value	Adjusted OR† (95% CI)	*p*-value
Sex					
Male	56	1.000		ni	
Female	49	0.657 (0.304–1.421)	0.286		
Age, years					
<50	15	1.000		1.000	
50–59	11	1.333 (0.242–7.348)	0.741	0.683 (0.067–6.973)	0.748
60–69	29	0.818 (0.221–3.031)	0.764	0.458 (0.050–4.158)	0.487
70–79	33	0.286 (0.079–1.034)	0.056	0.239 (0.035–1.613)	0.142
≥80	17	0.208 (0.047–0.931)	0.024	0.039 (0.030–0.603)	0.020
Lesion					
Cortical	7	1.000			
Cortico-subcortical	16	0.341 (0.055–2.131)	0.250		
Subcortical	44	0.750 (0.150–3.750)	0.726	ni	
Brain stem	19	2.812 (0.438–18.056)	0.276		
Cerebellum	3	0.375 (0.022–6.348)	0.497		
Multiple	16	0.450 (0.074–2.741)	0.386		
Laterality of lesion					
Right	54	1.000		1.000	
Left	51	1.718 (0.769–3.839)	0.187	2.179 (0.574–8.269)	0.252
Stroke type					
Ischaemic	85	1.000		ni	
Haemorrhagic	20	0.977 (0.369–2.587)	0.962		
DM					
(–)	77	1.000		ni	
(+)	28	1.184 (0.498–2.817)	0.702		
NIHSS at onset of rehabilitation					
<5	42	1.000		1.000	
≥5	49	0.109 (0.042–0.286)	<0.001	0.058 (0.012–0.287)	<0.001
MEP – Upper					
(+)	34	1.000		1.000	
(–)	71	0.508 (0.220–1.171)	0.112	2.411 (0.517–11.246)	0.263
MEP – Lower					
(+)	46	1.000		1.000	
(–)	59	0.341 (0.153–0.759)	0.008	0.366 (0.076–1.767)	0.211
SEP – Upper‡					
(+)	58	1.000		1.000	
(–)	44	0.227 (0.098–0.526)	0.001	0.584 (0.133–2.576)	0.478
SEP – Lower‡					
(+)	51	1.000		1.000	
(–)	49	0.167 (0.070–0.396)	<0.001	0.329 (0.094–1.159)	0.084
EP – Upper					
MEP (+) SEP (+)	28	1.000		1.000	
MEP (+) SEP (–)	3	0.947 (0.316–2.840)	0.923	2.755 (0.392–19.375)	0.309
MEP (–) SEP (+)	30	0.947 (0.076–11.870)	0.967	0.377 (0.007–20.126)	0.631
MEP (–) SEP (–)	41	0.196 (0.069–0.555)	0.002	0.925 (0.110–7.796)	0.943
EP – Lower					
MEP (+) SEP (+)	29	1.000		1.000	
MEP (+) SEP (–)	22	0.192 (0.050–0.739)	0.016	0.091 (0.010–0.820)	0.033
MEP (–) SEP (+)	13	0.071 (0.015–0.346)	0.001	0.057 (0.006–0.552)	0.013
MEP (–) SEP (–)	36	0.070 (0.020–0.251)	<0.001	0.099 (0.011–0.900)	0.040

*Unadjusted odds ratios by logistic regression analysis.

†Adjusted odds ratios by multivariate logistic regression analysis; adjusted for all other variables in model.

‡Three and 5 patients (upper limb and lower limb SEP study, respectively) were excluded because SEP study were impossible by their poor compliance.

CI: confidence interval; DM: diabetes mellitus; EP: evoked potentials; MEP: motor evoked potentials; ni: not included in the final adjusted model; NIHSS: National Institute of Health Stroke Scale; SEP: somatosensory evoked potentials.

MEP and SEP responses in the lower limbs during the sub-acute stage are less likely to achieve a good functional recovery during the chronic stage than those with positive MEP and SEP responses in the lower limbs.

To the best of our knowledge, this is the first study to use the cross-matched analysis of MEP and SEP to predict functional recovery after a stroke. Although MEP and SEP assess anatomically different pathways, both motor and sensory recoveries

Table III. *Contingency table for good functional recovery in relation to the presence of evoked responses*

Cut-off point of good functional recovery	Results of EPs		Functional recovery		Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
			Good, *n*	Poor, *n*				
mRS ≤2	MEP – Upper	(+)	21	13	39.6	75.0	61.8	54.9
		(–)	32	39				
	MEP – Lower	(+)	30	16	56.6	69.2	65.2	61.0
		(–)	23	36				
	SEP – Upper	(+)	39	19	73.6	61.2	67.2	68.2
		(–)	14	30				
	SEP – Lower	(+)	37	14	71.2	70.8	72.5	69.4
		(–)	15	34				
mRS ≤3	MEP – Upper	(+)	29	5	38.1	82.8	85.3	33.8
		(–)	47	24				
	MEP – Lower	(+)	37	9	48.7	69.0	80.4	33.9
		(–)	39	20				
	SEP – Upper	(+)	50	8	66.7	70.4	86.2	43.2
		(–)	25	19				
	SEP – Lower	(+)	46	5	63.0	81.5	90.2	44.9
		(–)	27	22				

EP: evoked potentials; mRS: modified Rankin Scale; MEP: motor evoked potentials; SEP: somatosensory evoked potentials.

after stroke are important, because they are integral aspects of a single functional activity. Therefore, considering both MEP and SEP would better predict functional recovery after a stroke than considering MEP or SEP alone. However, no previous study has considered MEP and SEP simultaneously.

In the present study, several demographic and neurophysiological variables were found to be significantly associated with functional recovery by unadjusted analysis. However, only age < 50 years, NIHSS at onset of rehabilitation < 5, and a positive response in lower limbs for MEP and SEP retained significance after adjusted analysis. The adjusted ORs for prediction of good functional recovery in Table II provide information on the relative effects of NIHSS and age vs EPs, showing that the relative contribution of EPs in predicting good functional recovery 3 months after a stroke is less than age or NIHSS. The adjusted ORs were age (0.039; ≥ 80 years vs < 50 years), NIHSS (0.058; ≥ 5 vs < 5), and EPs (0.099; lower MEP(–) SEP(–) vs lower MEP(+)SEP(+)).

Many studies have investigated the predictive value of MEP in terms of post-stroke functional recovery. Heald et al. (10) reported that the presence of MEP within 72 h of stroke onset can discriminate patients with high probabilities of survival and good functional recovery and, conversely, that its absence indicated poor recovery and an increased risk of death.

The predictive value of SEP for post-stroke functional recovery has also been well studied. Tzvetanov et al. (3) found that upper limb SEP amplitude recorded within 3 days of stroke onset provided significant prognostic information.

In the present study, only positive MEP and SEP responses in the lower limbs were found to be significantly related to a good functional recovery. Our explanation is that the dichotomous outcome measure (good or poor functional recovery) based on the mRS is probably too crude to reflect the effects of upper limb MEP and SEP findings. On the other hand, it is also possible that had we applied different mRS cut-off points for good and poor functional recovery our findings might have been different.

When the predictive value of EP study was calculated in terms of sensitivities and specificities, the specificity of MEP was found to be better than its sensitivity. However, this higher specificity was not significant in our SEP study. If the cut-off point for good functional recovery had been adjusted from mRS 2 to mRS 3, the positive predictive value of EP study would have increased to > 80%, but the negative predictive value would have decreased to < 50% (Table III). In this case, stroke patients with a positive response by EP study could be predicted to achieve a good functional recovery, but post-stroke prognosis could not be predicted in patients with a negative response. As a result of low negative predictive value of EP studies, the prediction of post-stroke functional recovery based on neurophysiological findings alone has its limitations. Therefore, we advise that other findings, both clinical and radiological, should also be considered, and that MEP and SEP should be considered complementary tests in terms of predicting functional recovery after stroke.

In conclusion, MEP and SEP studies performed during the sub-acute stage of stroke could be useful for predicting functional status during the chronic stage.

REFERENCES

1. Kwakkel G, Wagenaar RC, Kollen BJ, Lankhorst GJ. Predicting disability in stroke – a critical review of the literature. Age Ageing 1996; 25: 479–489.
2. Escudero JV, Sancho J, Bautista D, Escudero M, Lopez-Trigo J. Prognostic value of motor evoked potential obtained by transcranial magnetic brain stimulation in motor function recovery in patients with acute ischemic stroke. Stroke 1998; 29: 1854–1859.
3. Tzvetanov P, Rousseff RT, Atanassova P. Prognostic value of median and tibial somatosensory evoked potentials in acute stroke. Neurosci Lett 2005; 380: 99–104.
4. Huybrechts KF, Caro JJ. The Barthel Index and modified Rankin Scale as prognostic tools for long-term outcomes after stroke: a qualitative review of the literature. Curr Med Res Opin 2007; 23: 1627–1636.

5. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. Stroke 2007; 38: 1091–1096.
6. Gargano JW, Reeves MJ. Sex differences in stroke recovery and stroke-specific quality of life: results from a statewide stroke registry. Stroke 2007; 38: 2541–2548.
7. Rankin J. Cerebral vascular accidents in patients over the age of 60. III. Diagnosis and treatment. Scott Med J 1957; 2: 254–268.
8. Rossini PM, Barker AT, Berardelli A, Caramia MD, Caruso G, Cracco RQ, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: basic principles and procedures for routine clinical application. Report of an IFCN committee. Electroencephalogr Clin Neurophysiol 1994; 91: 79–92.
9. Rossini PM, Narici L, Martino G, Pasquarelli A, Peresson M, Pizzella V, et al. Analysis of interhemispheric asymmetries of somatosensory evoked magnetic fields to right and left median nerve stimulation. Electroencephalogr Clin Neurophysiol 1994; 91: 476–482.
10. Heald A, Bates D, Cartlidge NE, French JM, Miller S. Longitudinal study of central motor conduction time following stroke. 2. Central motor conduction measured within 72 h after stroke as a predictor of functional outcome at 12 months. Brain 1993; 116: 1371–1385.